erythroid hyperplasia with normal or low peripheral reticulocyte count; megaloblastic changes unresponsive to B_{12} or folic acid; ringed sideroblasts; bizarre erythroid maturation; megakaryocytes with one or two small, round nuclei and mature granular cytoplasm (if representing 25 percent of all megakaryocytes); giant platelets; platelets with granules; a left shift toward promyelocytes, and abnormalities of granulocytic maturation, including pelgeroid forms. At least two cell lines should be affected, each showing one or more of the mentioned abnormalities to establish the diagnosis of HD with confidence.

The correct diagnosis is important so that chemotherapy will be given promptly to patients with AML and withheld from those with HD. The distinction between the two identities is readily made by any competent hemotologist or pathologist familiar with the diagnostic criteria for AML. Referral of HD to centers participating in a registry of HD now being organized should eventually allow us to separate patients with "true preleukemia" from those who will progress to spontaneous cure and an intermediate group with a prolonged course of indeterminate duration.

At present there are no criteria available to predict the outcome in individual cases.

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REFERENCES

Hemopoietic Dysplasias (Preleukemic States)—A Symposium (From Blood Cells 2:1-2). New York City, Springer-Verlag, 1976

Block M, Jacobson LO, Bethard WF: Preleukemic acute human leukemia. JAMA 152:1018-1028, Jul 11, 1953

Bennett JM, Catovsky D, Daniel M-T, et al: Proposals for the classification of the acute leukaemias. Br J Haematol 33:451-458, Aug 1976

Bagby GC, Linman JW: Adrenal corticosteroid therapy in the preleukemic syndrome (hemopoietic dysplasia). Blood 50:182, Nov 1977

Current Status of Tests for Antinuclear Antibodies (ANA) in Rheumatic Diseases

ANTINUCLEAR ANTIBODIES (ANA) are present in the sera of many patients with systemic rheumatic diseases. The important specific antibodies to nuclear antigens are listed in Table 1.

The recommended tests for screening of patients' sera for ANA are the indirect immunofluorescent or immunoenzyme tests using rat or mouse kidney substrate tissue. The immunofluorescent test should involve a titering of positive cases with a description of nuclear staining patterns. Nuclear rim staining can be obtained with antibodies to double-stranded deoxyribonucleic acid (DNA) or to deoxyribonucleoprotein. Antibodies producing the speckled pattern of staining are those reacting with several nuclear protein antigens.

TABLE 1.—*Immunological Specificities of Antinuclear Antibodies*

Antibodies to deoxyribonucleic acid (DNA)
Reactive only with double-stranded DNA
Reactive with double and single-stranded DNA
Reactive with single-stranded DNA
Antibodies to deoxyribonucleoprotein (DNA-histone complex)
Antibodies to histones
Antibodies to nonhistone protein
Sm antigen (glycoprotein)
Ribonucleoprotein (RNP, ribonucleic acid (RNA)-protein complex)
SS-A (recognized by sera from Sjögren syndrome, chemical nature unknown)
SS-B (recognized by sera from Sjögren syndrome, chemical nature unknown)
Scl-1 (recognized by sera from scleroderma, chemical nature unknown)
Antibodies to nucleolar RNA (4-5S nucleolar RNA)

One must use other immunological tests besides an indirect immunofluorescent test to precisely identify the immunological specificities of ANA. The recommended test for antibodies to DNA is the radioimmunoassay procedure. Antibodies to DNA are present in many systemic rheumatic diseases and patients with systemic lupus erythematosus (SLE) usually have higher concentrations of DNA antibodies. Antibodies to Sm antigen and ribonucleoprotein (RNP) have been detected by passive hemagglutination, immunodiffusion and electroimmunodiffusion tests. Antibodies to Sm antigens have been shown to be highly specific for SLE and may be a serological marker for SLE. Antibodies to nuclear RNP have been found in several systemic rheumatic diseases; however, in patients with mixed connective tissue disease (MCTD), extremely high titers of RNP antibodies are seen.

More recently, an immunodiffusion test with antigens extracted from Wil_2 (a human lymphoblastoid tissue culture cell line) showed Sjögren syndrome has antibodies reacting with other nonhistone proteins.

In summary, one should use the indirect immunofluorescent screening test which will detect the presence of all types of ANA. Once the presence of ANA is noted, every effort should be made to identify the precise immunological specificity of

the ANA. Specific identification of ANA will aid in the differential diagnosis and management of the disease.

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REFERENCES

Notman DD, Kurata N, Tan EM: Profiles of antinuclear antibodies in systemic rheumatic diseases. Ann Intern Med 83:464-469, Oct 1975

Kurata N, Tan EM: Identification of antibodies to nuclear acidic antigens by counterimmunoelectrophoresis. Arthritis Rheum 19:574-580, May-Jun 1976

Alspaugh MA, Tan EM: Antibodies to cellular antigens in Sjögren's syndrome. J Clin Invest 55:1067-1073, May 1975

Alspaugh MA, Talal N, Tan EM: Differentiation and characterization of autoantibodies and their antigens in Sjögren's syndrome. Arthritis Rheum 19:216-222, Mar-Apr 1976

Alloimmune Neonatal Thrombocytopenia

ALLOIMMUNE neonatal thrombocytopenia (ANT) is an uncommonly reported disease. It is recognized in about one per 5,000 births, but it probably occurs much more frequently. ANT is analogous to Rh hemolytic disease of the newborn, except that the transplacentally acquired maternal antibody is directed against paternal antigens on the fetal platelets rather than on red cells. Usually the Pl^{A1} platelet antigen, present in 98 percent of the population, is involved.

The first-born infant has been affected in about half the reported cases. While petechiae, ecchymoses and purpura may appear at birth, more often these will develop several hours later. The platelet count is usually less than 30,000 per cu mm. The most serious threat to the infant is intracranial hemorrhage with possible neurologic injury or death.

Specific diagnosis of ANT is made difficult by the general unavailability and limited reliability of platelet antibody testing. Treatment can rarely await the establishment of the specific diagnosis, but must be instituted on the basis of a diagnosis of exclusion of other (and there are many) possible causes of neonatal thrombocytopenia.

Exchange transfusion to wash out the offending antibody has been tried with limited success. (The IgG antibody has about a 45 percent/55 percent intravascular/extravascular distribution and a half-life of 23 days.) The best therapy is probably transfusion with platelets lacking the Pl^{A1} antigen. Such platelets will be found in only 2 percent of the general population and platelet typing is not commonly available. The mother's platelets, however, will be compatible as she will lack the antigen against which she has formed the antibody (this will be true regardless of the antigen specificity).

It is essential that the maternal plasma be removed from the platelet preparation since maternal plasma is the source of the offending antibodies. The platelets can be suspended for infusion in group AB donor plasma.

With early diagnosis and appropriate therapy there should be rapid hematologic improvement. Occasional patients may require a second infusion of maternal platelets. Without treatment a mortality rate of about 14 percent has been reported in the literature.

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REFERENCES

Adner MM, Fisch GR, Starobin SG, et al: Use of "compatible" platelet transfusions in treatment of congenital isoimmune thrombocytopenic purpura. N Engl J Med 280:244-247, Jan 30, 1969

Aster RH: Thrombocytopenia due to enhanced platelet destruction, *In* Williams WJ, Beutler E, Erslev A, et al (Eds): Hematology, New York City, McGraw-Hill Book Company, 1972, pp 1131-1158

Amyloid Fibrils in Urine

AMYLOIDOSIS is a connective tissue disease, first described by Virchow, in which deposits of a hyaline protein carbohydrate material are laid down between the parenchymal cells of various organs, gradually infiltrating them and preventing their normal function. Blood vessel walls are especially susceptible to amyloid and it is in these areas that it can initially be seen in histological sections.

For diagnosis, a rectal biopsy can be done in the operating room, or a renal biopsy may be done using fluoroscopy. However, both of these procedures involve patient discomfort and major operating room costs. Such invasive procedures run the risk of serious internal bleeding. The negative results often obtained to not rule out amyloid and most physicians, in view of the pain and hazard involved, are loath to repeat the procedure.

Recently, a new technique has been evolved using the patient's urine sediment examined by electron microscopy. A 250 to 400 ml quantity of clean-catch urine, collected without preservatives, is spun at 10,000 G for one hour and the sediment obtained is fixed in buffered 2 percent glutaraldehyde or buffered 4 percent paraformaldehyde. The